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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,758	10/14/2005	M. Dean Savage	F-PRCB-05	1329

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EXAMINER	
MARTIN, PAUL C	

ART UNIT	PAPER NUMBER
1655	

DATE MAILED: 06/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/517,758	SAVAGE, M. DEAN	
	Examiner	Art Unit	
	Paul C. Martin	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 December 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/13/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-24 are pending in this application and were examined on their merits.

Specification

The use of the trademarks Bodipy and Costar has been noted in this application. It should be capitalized wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101, which states "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-14, 22, 23 and 24 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-11, 28, 37, 63 and 64 of copending Application No. 10/865,893. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claims 15-21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 29, 32, 34, 35, 37 and 38 of copending Application No. 10/865,893. Although the conflicting claims are not identical, they are not patentably distinct from each other; the claims of '758 'anticipate' Instant claims 15-21 due to the fact that they teach every limitation of Instant claims 15-21.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Objections

Claim 11 is objected to because of the following informalities: The word "be" in line 2 of the claim should be deleted for purposes of clarity if Applicant intended the phrase to read, "...bound to the target group". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14, 19 and 22-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for kinases, phosphatases and proteases, does not reasonably provide enablement for all possible enzymes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. There is no guidance or direction presented to direct one to determine which enzymes would work in the broadly claimed invention, which is a complex and unpredictable art. Therefore because of the large number of inoperable embodiments claimed, the ordinary artisan would be subjected to undue experimentation to practice the claimed invention.

For example, the claimed term "enzyme" encompasses such proteins with diverse activities such as ligases, oxidoreductases, polymerases, lyases and isomerases just to name a few. Nowhere in the instant disclosure, or in any example, is it taught or suggested the use of other enzymes beyond those that fall in the above classes. One skilled in the art would be subjected to needless experimentation in trying to adapt the claimed invention to any enzyme beyond those taught in the instant specification, due to the disparate catalytic activities and functions of enzymes beyond the scope taught by the Applicant. It is therefore deemed that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 19-22 recite the limitation "endproduct" in line 1 of the claims. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 4-6, 8, 9, 11-13 are rejected under 35 U.S.C. 102(e) as being anticipated by Nikiforov (US 6,699,655 B2) as evidenced by Cox *et al.* (US 5,034,189)✱).

Nikiforov teaches a composition comprising a fluorescently labeled kinase substrate, and a phosphate donor, and a binding component comprising multivalent (paramagnetic) metal ions (selected from the group consisting of Fe^{3+}, Ca^{2+}, Ni^{2+}, and Zn^{2+}) chelated to the binding component which binds to a fluorescently labeled phosphorylated product and induces a shift in the polarized fluorescence emitted from the mixture, the level of polarized fluorescence being indicative of an amount of fluorescently labeled phosphorylated product being formed by the kinase reaction (Column 29, Claims 1, 3, 4 and 6-9).

It is inherent in the method of Nikiforov that the multivalent metal ions would bind the phosphoryl group, as Nikiforov teaches they have significant binding affinity for phosphorylated substrates (Column 13, Lines 54-62) and that the binding of multivalent (paramagnetic) metal ions to a fluorescently labeled phosphorylated product will quench the fluorescence as evidenced by Cox *et al.* (US 5,034,189)✱ Column 13, Lines 66-68 and Column 14, Lines 1-4.

Claims 1, 2, 4-6, 8, 9 and 11-13 are rejected under 35 U.S.C. 102(e) as being anticipated by Nikiforov (US 6,472,141 B2) as evidenced by Cox *et al.* (US 5,034,189)✱).

Nikiforov teaches a composition comprising a fluorescently labeled kinase substrate, and a phosphate donor, a product resulting from the kinase enzyme reacting with the kinase substrate and phosphate donor, and a binding component comprising multivalent (paramagnetic) metal ions (selected from the group consisting of Fe^{3+}, Ca^{2+}, Ni^{2+}, and Zn^{2+}) chelated to the binding component which binds to a fluorescently labeled phosphorylated product and induces a shift in the polarized fluorescence emitted from the mixture, the level of polarized fluorescence being indicative of an amount of fluorescently labeled phosphorylated product being formed by the kinase reaction (Column 38, Claims 18, 21 and 22).

It is inherent in the method of Nikiforov that the multivalent metal ions would bind the phosphoryl group, as Nikiforov teaches they have significant binding affinity for phosphorylated substrates (Column 14, Lines 44-50) and that the binding of multivalent (paramagnetic) metal ions to a fluorescently labeled phosphorylated product will quench the fluorescence as evidenced by Cox *et al.* (US 5,034,189)✱ Column 13, Lines 66-68 and Column 14, Lines 1-4.

✱ This reference is being cited to rely an inherent property of the composition and is not used in the basis for rejection *per se*.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nikiforov (US 6,472,141 B2) as evidenced by Cox *et al.* (US 5,034,189)✱).

The teachings of Nikiforov were discussed above.

Nikiforov does not teach a method wherein the target group is an imidazole, wherein the enzyme is a phosphatase, wherein the observed fluorescence from the mixture is related to that of an external reference wherein a differential fluorescent signal, if any, between the two is indicative of the final state of the fluorophore labeled substrate population after enzymatic reaction and in turn an indicator of enzymatic activity.

Nikiforov does not teach a kit comprising a paramagnetic metal ion and instructions for use of the kit and including a synthetic calibrator.

Nikiforov suggests the use of the method with phosphatase enzymes and the comparison of the observed fluorescence to an external reference control wherein a differential fluorescent signal, if any, between the two is indicative of the final state of the fluorophore labeled substrate population after enzymatic reaction and in turn an indicator of enzymatic activity (Column 27, Lines 28-45 and Fig. 19).

Nikiforov teaches a kit for carrying out the method comprising reagents (labeled substrate and polyionic compound) and instructions for use (Column 25, Lines 9-26).

It would have been obvious to one of ordinary skill in the art to modify the method of Nikiforov to include the use of imidizole as a target group because Nikiforov teaches that paramagnetic metal ions have strong affinities for nitrogen groups, imidazole being composed of 3 carbons, 4 hydrogens and 2 nitrogens, therefore the use of imidazole would have been an obvious variant of the phosphorylated target group because paramagnetic ions are strongly attracted to both targets. It would have been obvious to one of ordinary skill in the art to compare the observed fluorescence to an external reference control wherein a differential fluorescent signal, if any, between the two is indicative of the final state of the fluorophore labeled substrate population after enzymatic reaction and in turn an indicator of enzymatic activity because this would allow one to verify that a reaction was in fact taking place and to observe the rate and final change in fluorescence over time between a control and experimental assay. It would have further been obvious to compile a kit containing the necessary reaction components and a synthetic calibrator as a more reliable means of establishing a reference. Synthetic calibrators could be manufactured with a high degree of accuracy and reliability and would ensure consistent results over many uses and between individual kits. One of ordinary skill in the art would have been motivated to make these adaptations in order to be assured of the highest degree of accuracy in the experiment as well as improve the speed and efficiency with which it was carried out. There would have been a reasonable expectation of success because Nikiforov teaches or suggests all of the above adaptations and those not specifically taught would have been obvious to one of skill in the art as reasoned above.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Nikiforov (US 6,689,565 B2) teaches a kit containing paramagnetic metal ions and instructions for use.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one with ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence or evidence to the contrary.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul C. Martin whose telephone number is 571-272-3348. The examiner can normally be reached on M-F 8am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Paul Martin
Examiner
Art Unit 1655

06/22/06

PATRICIA LEITH
PRIMARY EXAMINER